

# The effect of supplementation of *Lactobacillus paracasei* HII01 on salivary cortisol, and dehydroepiandrosterone sulfate (DHEA-S) levels



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## ABSTRACT

**Background:** Fatigue is one of the serious health issues, and stress is the main factor that induces chronic fatigue syndrome (CFS). The dysregulation of stress management pathway may account for the development of CFS. The human body comprises several neurobiological networks to manage physical and emotional insults. Hypothalamic-pituitary-adrenal (HPA) axis is one of the important neuroendocrine networks involved in the neurophysiological activity of the host system. The response of HPA axis depends on the physical and psychological state of stress and other factors like time and duration of stress. The probiotic supplements are proved as an adjuvant therapeutic agent for several diseases. **Aims and Objective:** The aim of the current study was to evaluate the effect of *Lactobacillus paracasei* HII01 supplementation on salivary cortisol and DHEA-S levels of fatigue subjects. **Materials and Methods:** After 12-weeks of probiotic intervention significantly reduced the salivary cortisol level, while DHEA-S level was not affected. The ratio of cortisol: DHEA-S was reduced after probiotic intervention. **Results:** The results concluded that *L. paracasei* HII01 has the ability to reduce the stress level in fatigue subjects by reducing the salivary cortisol level. **Conclusion:** The results evidently to recommend that the ingestion of 12.5 billion CFU of *L. paracasei* HII01 per day for 12 weeks significantly amended HPA-Axis by lowering salivary cortisol and ratio cortisol: DHEA-S in fatigue subjects.

**Key words:** Probiotics; *Lactobacillus paracasei*; Fatigue; Stress; Cortisol; HPA-Axis.

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## INTRODUCTION

Chronic fatigue syndrome (CFS) is one of the unbearable neurological diseases.<sup>1</sup> Defects in memory, concentration, sleep pattern, muscular-skeletal pain, and constant fatigue are the common symptoms of CFS.<sup>2</sup> The severity of the symptoms is unique among the patients, and some of the patients can manage their symptoms by restricting their energy needs.<sup>3</sup> The underlying mechanism and cause of CFS were not yet elucidated.

The defect in regulation of stress management pathway may responsible for the development of CFS.<sup>1,3</sup> Human

body comprises several neurobiological networks to manage stress. Hypothalamic-pituitary-adrenal (HPA) axis is one of the important neurological axes having role in stress response, and maintaining the homeostasis. The response of HPA axis depends on the physical and psychological state of stress and other factors like time and duration of stress.<sup>4-7</sup>

The gut microbiota has direct influence on HPA axis and neuroendocrine system.<sup>8,9</sup> The changes in the gut microbial composition will affect the psychological well-being, which is now considered as a complementary therapeutic approach to treat psychological disorders like depression

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and anxiety.<sup>10</sup> The oral administration of potent microbes, generally probiotics, are proven as adjuvant therapeutic method for several diseases and disorders.<sup>11-16</sup> It has been reported that the supplementation of probiotics improved the human mental health status.<sup>17</sup>

Cortisol is hormone, which helps coping stress, released by the adrenal glands with the response to corticotrophin-releasing factor. The stress hormone levels were increased up to two-five folds during stress.<sup>18</sup> The adrenal glands also produce hormone dehydroepiandrosterone-S (DHEA-S). DHEA-S is believed as one of the stress-responsive hormones. The low level of DHEA-S associated with increased psychological illness and stress.<sup>19</sup> The objective of the current study was to evaluate the effect of *Lactobacillus paracasei* HII01 supplementation on salivary cortisol and DHEA-S levels of fatigue subjects.

## MATERIALS AND METHODS

### Preparation and intervention of probiotics

The probiotic strain *Lactobacillus paracasei* HII01 was cultured and lyophilized at Lactomason Co., Ltd., South Korea. The live powdered probiotic strain was used for the study. The sachet containing  $12.5 \times 10^{10}$  CFU/g of *L. paracasei* HII01 was given to volunteers and insisted them to consume for twelve weeks (one sachet per day).

### Measurement of cortisol and DHEA-Sulfate level

The saliva samples were collected from the volunteers at baseline and after twelve weeks of intervention at 7-9 am and stored at 4°C until use. The salivary cortisol and DHEA-S levels were measured by the ELISA method using The Eagle Biosciences Salivary Cortisol ELISA Assay kit as per the manufacturer's instructions.

### Statistical analysis

The statistical program STATA15 was used for the data analysis. The Paired-sample t-test was used to distinguish within-group differences.

## RESULTS

### Demographic information of the subjects

Nine volunteers participated in the study. The mean age and BMI of the participants were  $48.33 \pm 15.69$  years, and  $27.91 \pm 3.05$  kg/m<sup>2</sup> at the time of study, respectively (Table 1).

### Changes in Salivary Cortisol, and DHEA-S levels

The salivary cortisol level at baseline and after treatment was  $202.78 \pm 84.32$  and  $156.24 \pm 61.96$  ng/ml, respectively. The salivary cortisol level was significantly ( $p = 0.003$ ) decreased, after the probiotic intervention. Whereas, the DHEA-S level

was not affected by the probiotic intervention. The level of DHEA-S was  $0.71 \pm 0.42$  and  $0.71 \pm 0.45$  ng/ml at baseline and after treatment, respectively (Table 2).

### Changes in Ratio of Cortisol: DHEA-S

The ratio of cortisol: DHEA-S at baseline and after probiotic treatment was  $460.61 \pm 409.30$ , and  $374.14 \pm 381.52$  ng/ml, respectively. The probiotic supplementation significantly ( $p = 0.011$ ) reduced the ratio of cortisol: DHEA-S (Table 2).

## DISCUSSION

The studies on the beneficial effect of probiotic supplementation on mental status of fatigue subjects are very limited. The current study revealed that the twelve-week supplementation of *L. paracasei* HII01 effectively reduced the salivary cortisol level (Table 2), which indicated that the stress level has been reduced after the probiotic intervention.

The previous studies reported that the consumption of *L. helveticus* R0052 and *Bifidobacterium longum* R0175 for thirty days reduced the urine cortisol level,<sup>10</sup> and the strain *L. gasseri* CP2305 reduced the salivary cortisol level after 4 weeks of consumption.<sup>20</sup>

There was no change in the DHEA-S level in fatigue subjects after twelve-weeks of *L. paracasei* HII01 supplementation. The ratio of cortisol: DHEA-S was reduced after the probiotic intervention (Table 2).

**Table 1: Demographic Information of the Subjects Participated in the Study**

Characteristic	Number (Percentage)
Gender	
Male	4 (44.4)
Female	5 (55.6)
Age (Years)	
≤30	2 (22.2)
31-59	4 (44.5)
60 or more	3 (33.3)
Total (Mean±SD)	9 (48.33±15.69)
BMI	
<25	2 (22.2)
≥25	7 (77.8)
Total (Mean±SD)	9 (27.91±3.05)

**Table 2: The changes in salivary cortisol and DHEA-S levels after probiotics intervention**

Biomarkers	Baseline (ng/ml)	After 12 weeks (ng/ml)	p-value
Salivary Cortisol	202.78±84.32	156.24 ± 61.96	0.003
Salivary DHEA-S	0.71±0.42	0.71 ± 0.45	1.00
Cortisol :DHEA-S ratio	460.61±409.30	374.14 ± 381.52	0.011

The beneficial effect of probiotic supplementation depends on the strain, concentration, duration, and other aided activities. The single strain of probiotic *L. gasseri* CP2305 showed positive effects on stress management,<sup>20</sup> and multi-strain probiotic supplementation (*L. helveticus* R0052 and *B. longum* R0175) also reduced the stress.<sup>10</sup>

The current study was an initial clinical trial on the effect of *L. paracasei* HII01 on stress management in fatigue subjects. It has some disadvantages such as very limited number of subjects, limited analyzed parameters, no placebo control, and subjects with different lifestyles. The further extended study is needed to uncover the favorable impact of *L. paracasei* HII01 on stress management in fatigue subjects.

## CONCLUSION

The results evidently to recommend that the ingestion of 12.5 billion CFU of *L. paracasei* HII01 per day for 12 weeks significantly amended HPA-Axis by lowering salivary cortisol and ratio cortisol: DHEA-S in fatigue subjects. However, the results of the current study need to be validated with an increased number of subjects and placebo control since the present study has some limitations.

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**Authors Contribution:**

**EL-** Concept and design of the study, statistically analyzed and interpreted, manuscript preparation; **BSS-** Statistically analyzed and interpreted, manuscript preparation, critical revision of the manuscript; **SS-** Concept and design of the study, statistically analyzed and interpreted; **PS-** Manuscript preparation, critical revision of the manuscript; **SP-** Concept and design of the study; **CC-** Concept and design of the study, statistically analyzed and interpreted, manuscript preparation, critical revision of the manuscript

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